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IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

HORIZON PHARMA IRELAND LIMITED, HZNP LIMITED and HORIZON PHARMA USA, INC.,
Plaintiffs,
v.
ACTAVIS LABORATORIES UT, INC.,
Defendant.

C.A. Nos. 1:14-cv-07992-NLH-AMD
(Consolidated with C.A. Nos. 15-5025, 15-6131, and 15-6989)

Hon. Noel L. Hillman, U.S.D.J.

Hon. Ann Marie Donio, U.S.M.J.

[redacted]

DEFENDANT ACTAVIS LABORATORIES UT, INC.'S LOCAL RULE 56.1 STATEMENT OF MATERIAL FACTS NOT IN DISPUTE IN SUPPORT OF ITS MOTION FOR SUMMARY JUDGMENT OF NON-INFRINGEMENT OF U.S. PATENT NOS. 8,217,078, 8,546,450, AND 9,132,110

Defendant Actavis Laboratories UT, Inc. ("Actavis") submits this Statement of Material Facts Not in Dispute pursuant to Rule 56.1 of the Local Civil Rules of the United States District Court for the District of New Jersey.

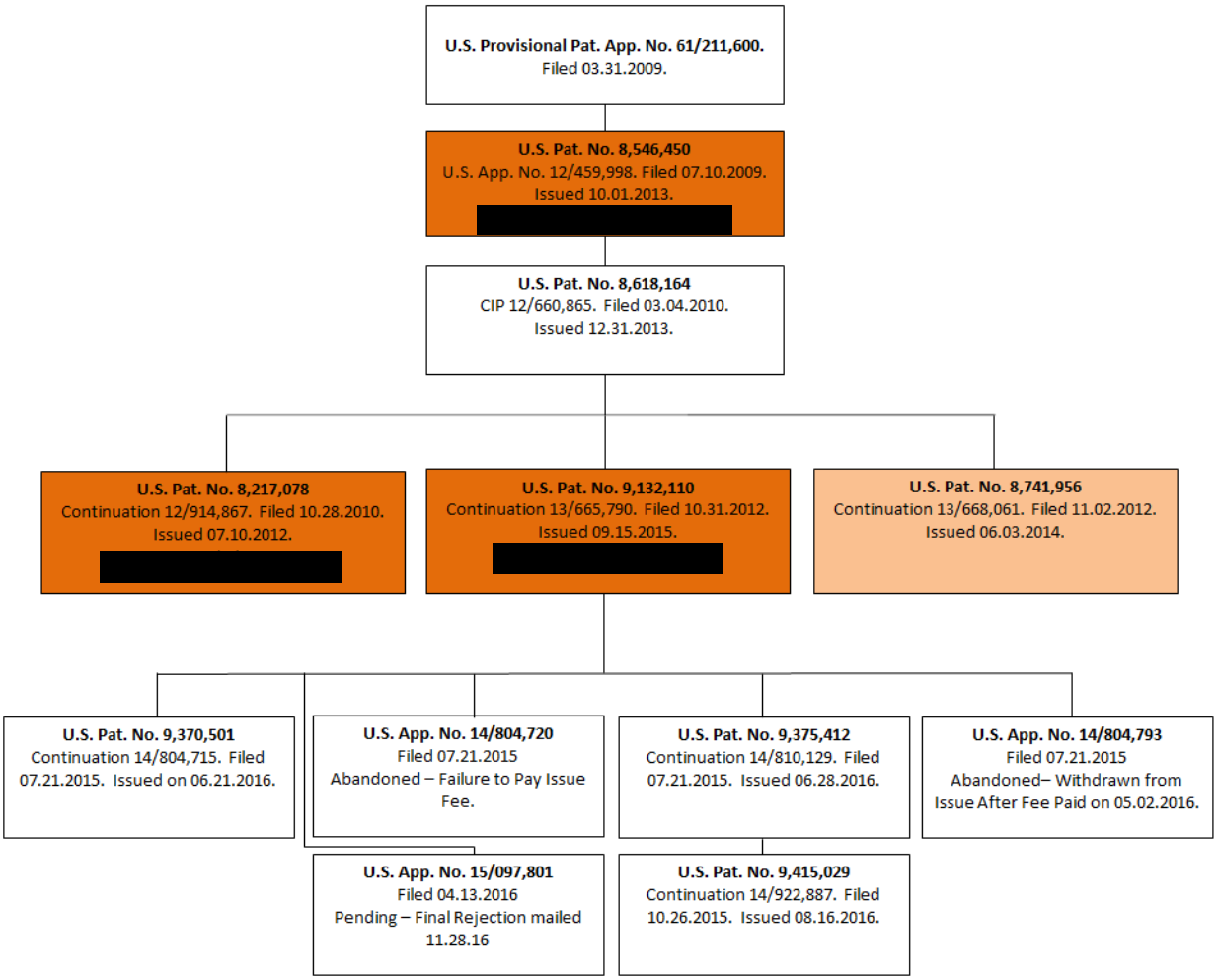
I. HORIZON'S PATENTS: THE '450 PATENT FAMILY

1. HZNP Limited is the owner of U.S. Patent Nos. 8,546,450 ("the '450 patent"), 8,217,078 ("the '078 patent"), and 9,132,110 ("the '110 patent") (collectively, "asserted method patents"). (No. 14-cv-7992, Dkt. 1, Compl. ¶¶ 36, 38; No. 15-cv-06989, Dkt. 1, Compl. ¶43.)

2. Each of the asserted method patents discloses methods for applying topical formulation containing diclofenac sodium to treat pain associated with osteoarthritis of the knee. (Ex.[1] 2, '450 patent, abstract, [redacted]

3. The following family tree illustrates the relationship between the '450, '078, and '110 patents, each of which is shaded in dark orange.

[1] "Ex." refers to the corresponding exhibit attached to the Declaration of Andrew S. McElligott, filed concurrently herewith.



4. Each of the patents shaded in orange in the family tree of Paragraph 3 is listed in the FDA Publication *Approved Drug Products with Therapeutic Equivalence Evaluations* in connection with Pennsaid® 2%. *Approved Drug Products with Therapeutic Equivalence Evaluations* is also known as the "Orange Book."

5. In addition to the four patents shaded in the family tree in Paragraph 3 above, another fourteen patents are listed in the Orange Book in connection with Pennsaid 2%. (Ex. 3, Current Orange Book Listing.) Thus, a total of eighteen patents are listed in the Orange Book in connection with Pennsaid 2%.

6. The fourteen patents listed in the Orange Book that are not shaded in Paragraph 3 include U.S. Patent No. 8,252,838 ("'838 patent") and nine patents related to the '838 patent as well as several patents that are listed in Paragraph 3 but are not shaded, specifically, U.S. Patent Nos. 9,370,501, 9,375,412, 9,415,029, and U.S. Patent No. 8,618,164. (Ex. 3, Current Orange Book Listing.)

7. The patents listed in the Orange Book fall into two patent families – the '838 formulation patent family and the '450 method of treatment patent family, which are the patents identified in the family tree of Paragraph 3.

8. U.S. Patent No. 8,741,956 ("'956 patent") is shaded in light orange in the family tree in Paragraph 3 and was the subject of cross-motions to dismiss and for summary judgment in the above captioned action. (Dkt. 153, 164.)

9. [redacted] the parties submitted and the Court entered a stipulated dismissal of Actavis's Thirteenth and Fourteenth Counterclaims seeking a Declaration of Non-Infringement and Invalidity of the '956 patent. (Dkt. 243, ¶ 1.) On January 11, 2017, Horizon's Motion to Dismiss Actavis's Thirteenth and Fourteenth Counterclaims (Dkt. 153) and Actavis's Cross-Motion for Summary Judgment of Non-Infringement of the '956 Patent (Dkt. 164) were deemed moot and accordingly terminated pursuant to the same stipulation.

A. Overview of Asserted Patents and Claims

10. [redacted]

11. Horizon's infringement contentions allege indirect infringement in the form of both induced infringement under 35 U.S.C. § 271(b) and contributory infringement under 35 U.S.C. § 271(c). (Ex. 6, July 13, 2015 Infringement Contentions at 4.)

12. [redacted]

13. [redacted]

14. As a result of Horizon's service of its Amended Disclosure of Asserted Claims on January 9, 2017, no claims of the '164 patent are asserted against Actavis. (Ex. 7, Jan. 9, 2017, Pls. Amended Disclosure of Asserted Claims.)

1. U.S. Patent No. 8,546,450

15. The '450 patent issued from U.S. Patent Application No. 12/459,998 ("the '998 application"), which was filed on July 10, 2009 (Ex. 2, '450 patent; Ex. 8, '998 File History, Bibliographic Data Sheet (ACT-PENN0003539).)

16. [redacted]

17. [redacted]

[redacted]

2. U.S. Patent No. 8,217,078

19. The ’078 patent issued from U.S. Patent Application No. 12/914,867 (“the ’867 application”), which was filed on October 28, 2010 (Ex. 9, ’078 Patent; Ex. 10, ’867 File History, Bibliographic Data Sheet (ACT-PENN0006904).) The ’867 application is a continuation of U.S. Patent Application No. 12/660,865 (“the ’865 application”), which was filed on March 4, 2010, and is a continuation-in-part of the ’998 application. (Ex. 11, ’164 Patent; Ex. 12, ’865 File History, Bibliographic Data Sheet (ACT-PENN0006180).)

20. [redacted]

[redacted]

21. [redacted]

[redacted]

22. [redacted]

[redacted]

23. [redacted]

[redacted]

3. U.S. Patent No. 9,132,110

24. The ’110 patent issued from U.S. Patent Application No. 13/665,790 (“the ’790 application”), which is a continuation of the ’865 application and was filed on October 31, 2012. (Ex. 14, ’110 Patent; Ex. 15, ’790 File History, Bibliographic Data Sheet (ACT-PENN0015130.)

25. The written description of the ’110 patent is materially identical to the written description of the ’078 patent. (*Compare* Ex. 9, ’078 patent *with* Ex. 14, ’110 patent.)

26. Claims 1, 10, 12 and 14 are the only independent claims of the ’110 patent. [redacted]

[redacted]

27. [redacted]

[redacted]

B. Limitations Requiring A Second Topical Substance

31. Each of the eight asserted claims requires the application of a topical diclofenac sodium formulation that contains dimethylsulfoxide ("DMSO") and the subsequent application of a second topical substance, which must be either a sunscreen, insect repellent, or topical medication, "during the course of treatment" of osteoarthritis of the knee.

1. Limitations Requiring Application Of A Second Topical Medication

32. Asserted claims [redacted] ach recite the application of a second topical medication in addition to a topical diclofenac preparation. [redacted]

33. [redacted]

34. [redacted]

35. [redacted]

[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]

[redacted]

a. Claims reciting that the second topical medication be a corticosteroid

36. [redacted]

37. There are just four mentions of corticosteroids in the written description of the '078 patent, which are reproduced below:

- "5.14 Corticosteroid Treatment" (Ex. 9, '078 patent, col. 61, l. 22.)
- "Other factors that increase the risk of GI bleeding in patients treated with NSAIDs include concomitant use of oral corticosteroids or anticoagulants, longer duration of NSAID therapy, smoking, use of alcohol, older age, and poor general health status." (*Id.*, col. 64, ll. 1-6.)
- 5.14 Corticosteroid Treatment
  PENNSAID Topical Solution cannot be expected to substitute for corticosteroids or to treat corticosteroid insufficiency. Abrupt discontinuation of corticosteroids may lead to exacerbation of corticosteroid-response illness. For patients on prolonged corticosteroid therapy, taper slowly if a decision is made to discontinue corticosteroids. (*Id.*, col. 67, ll. 1-8.)
- The chance of a person getting an ulcer or bleeding increases with:
  taking medicines called "corticosteroids" and "anticoagulants" (*Id.*, col. 77, ll. 46-49.)

38. All mentions of corticosteroids in the written description of the '078 patent appear in the "Attachment" at the end of the written description. (Ex. 9, '078 patent, col. 58, l. 60-col. 80, l. 33.)

39. All references to corticosteroids in the written description of the '078 patent either expressly reference oral corticosteroids or are silent as to the form of administration. (Ex. 9, '078 patent, col. 61, l. 22, col. 64, ll. 1-6, col. 67, ll. 1-8, col.77, ll. 46-49.)

40. There is no mention of a "topical corticosteroid" anywhere in the specification of the '078 patent. (Ex. 9, '078 patent.)

41. The words "topical" and "corticosteroid" never appear in the same sentence anywhere in the written description of the '078 patent. (Ex. 9, '078 patent.)

b. Claims reciting that the second topical medication be tretinoin or minoxidil

42. Several claims of the ’110 and ’078 patents recite the application of a second topical medication and state that the medication may be tretinoin or minoxidil. (Ex. 14, ’110 patent, claim 14; Ex. 9, ’078 patent, claims 1, 12.)

43. [redacted]

44. Tretinoin is the active ingredient in Retin-A®. (Ex. 9, ’078 patent, col. 39, ll. 13-15.)

45. Retin-A® is indicated for treatment of acne vulgaris. (Ex. 17, Retin-A Label, p. 1 (ACT-PENN0011740); Ex. 18, Pappagallo Dep. Tr. 289:24-290:4)

46. Retin-A® has no other indicated use other than for the treatment of acne vulgaris. (Ex. 17, Retin-A Label, p. 1 (ACT-PENN0011740).)

47. Minoxidil is the active ingredient in Men’s Rogaine® Extra Strength Topical Solution. (Ex. 9, ’078 patent, col. 39, ll. 15-16.)

48. Men’s Rogain® Extra Strength Topical Solution has no indicated use other than for hair growth on the scalp. (Ex. 19, Rogaine Label, ACT-PENN0011753; Ex. 18, Pappagallo Dep. Tr. 290:5-10.)

49. Example 2 of the ’078 patent describes using tretinoin and minoxidil as controls in testing on the influence of topical diclofenac solution containing 1.5% diclofenac sodium on

the percutaneous absorption of three environmental toxins. (Ex. 9, '078 patent, col. 38, l. 54-col. 39, l. 37.)

50. Example 2 of the '078 patent reports a study in which female Göttingen Minipigs ("minipigs") were administered two different topical substances. (Ex. 9, '078 patent, col. 39, ll. 29-37.) Each animal received one of three "toxins," specifically oxybenzone, N-N-diethyl-m-toluamide, or 2,4-D dimethylamine salt. (*Id.*, col. 39, ll. 6-13, col. 39, ll. 38-42.) Each animal also was administered either topical diclofenac solution or one of two "control" substances, specifically Retin®-A or Rogaine®. (*Id.*, col. 39, ll. 14-17.)

51. The two topical "control" substances were applied to exactly the same administration site on the minipigs as the toxins. (Ex. 9, '078 patent, col. 40, ll. 41-44; Ex. 20, Pappagallo Reply Rep. ¶ 25.)

52. N-N-diethyl-m-toluamide is also known as "DEET," and is used as an insect repellant. (Ex. 9, '078 patent, col. 43, ll. 11-13.)

53. 2,4-D dimethylamine salt is used as a herbicide. (Ex. 9, '078 patent, col. 43, ll. 13-16; Ex. 21, Pesticide Guide.)

54. The table below shows which substances were administered to each group of pigs in Example 2:

Group	Toxin No. (Name)	Test Item/Control
1	1 (oxybenzone)	Topical Diclofenac Solution (Test Item)
2	2 (DEET)	Topical Diclofenac Solution (Test Item)
3	3 (2,4-D)	Topical Diclofenac Solution (Test Item)
4	1 (oxybenzone)	Retin-A (Control no. 1)
5	2 (DEET)	Rogaine ® (Control no. 2)
6	3 (2,4-D)	Rogaine ® (Control no. 2)

(Ex. 9, '078 patent, col. 40, ll. 14-22.)

55. Example 3 of the ’078 patent describes a study in which minipigs were administered two different topical substances using similar methods as Example 2. (Ex. 9, ’078 patent, col. 43, ll. 18-24.) Like Example 2, each minipig in Example 3 received: (i) either topical diclofenac sodium or a “control”; and (ii) a “toxin.” (*Id*.)

56. Example 3 of the ’078 patent differs from Example 2 of the ’078 in a few respects. First, the sole “control” used was Retin-A 0.1%. (Ex. 9, ’078 patent, col. 43, ll. 16-17.) Second, only two “toxins” were used in Example 3: (i) DEET; and (ii) 2, 4-D. (*Id*., col. 43, ll. 11-17.) Third, the minipigs in Example 3 received a different amount of “toxin” than the minipigs in Example 2. (*Id*., col. 43, ll. 31-34.) Specifically, minipigs in Example 3 received 1.5 mL of the “toxin.” For those minipigs in Example 2 that received DEET and 2,4-D, the amount administered was either 1.08 mL or 0.88 mL, respectively. (*Id*., col. 39, ll. 53-56.)

57. Examples 2 and 3 of the ’078 patent do not describe any animals that received both topical diclofenac sodium and also one of the controls. (Ex. 9, ’078 patent, col. 38, l. 54-col. 44, l. 35.)

58. None of the animals tested in Examples 2 and 3 of the ’078 patent received both topical diclofenac sodium and Retin®-A (tretinoin). (Ex. 9, ’078 patent, col. 38, l. 54-col. 44, l. 35.)

59. None of the animals tested in Examples 2 and 3 of the ’078 patent received both topical diclofenac sodium and Rogaine® (minoxidil). (Ex. 9, ’078 patent, col. 38, l. 54-col. 44, l. 35.)

60. There is no mention anywhere in the written description of the ’078 patent of administering both topical diclofenac sodium and tretinoin. (Ex. 9, ’078 patent.)

61. There is no mention anywhere in the written description of the '078 patent of administering both topical diclofenac sodium and minoxidil. (Ex. 9, '078 patent.)

62. The disclosures in the written descriptions of the '078 and '110 patents relating to tretinoin and minoxidil are substantively identical. (*Compare* Ex. 9, '078 patent *with* Ex. 14, '110 patent.)

63. When asked whether he would ever apply tretinoin to the knee, Horizon's expert, Dr. Marco Pappagallo admitted, "[p]robably not." (Ex. 18, Pappagallo Dep. Tr. 289:24-290:4.)

64. When asked whether he could "imagine any situation where a patient might apply acne medication to their knee," Dr. Pappagallo responded, "[n]o." (Ex. 18, Pappagallo Dep. Tr. 290:5-8.)

65. When asked whether there would be any reason to apply minoxidil to the knee, Dr. Pappagallo responded, "[f]or osteoarthritis, no. Or for any condition of the knee." (Ex. 18, Pappagallo Dep. Tr. 290:11-14.)

66. Horizon does not allege that any patient would apply Actavis's ANDA product to the knee and then also apply either tretinoin or minoxidil. (Ex. 18, Pappagallo Dep. Tr. 289:24-290:17; *see generally* Ex. 16, Pappagallo Rep.; Ex. 20, Pappagallo Reply Rep.)

2. Limitations Requiring Application Of Sunscreen Or Insect Repellant Claims

67. [redacted]

68. [redacted]

[redacted]

69. [redacted]

70. [redacted]

71. [redacted]

72. [redacted]

[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]

[redacted]

73. The specification of the '450 and '110 patents repeatedly describes oxybenzone, which is the active compound in some sunscreens, as a "toxin." (Ex. 2, '450 patent, col. 35, ll. 48-55; Ex. 14, '110 patent, col. 39, ll. 49-56.) The specification also refers to "sunscreen" itself as a "toxin." The '450 patent specification states in relevant part:

- "The environmental toxins selected for use in the study were oxybenzone (in the form of Equaline SPF 23 face sunscreen; active compound 6% oxybenzone) . . . ." (Ex. 2, '450 patent, col. 35, ll. 48-50.)
- "The Test Item and the controls were supplied ready-to-use. Toxin No. I (sunscreen) was applied undiluted." (Ex. 2, '450 patent, col. 36, ll. 13-14.)
- "In contrast, the exposure to oxybenzone could be well quantified on all application days. The courses of the plasma concentrations of oxybenzone were summarized non-compartmentally by means of C_{max} (maximum observed plasma concentration), tmax (time of C_{max} after application of the toxin) . . . ." (Ex. 2, '450 patent, col. 38, ll. 40-45.)
- "Topical Diclofenac sodium, however, did not amplify the exposure of oxybenzone, an epicutaneoulsy applied toxin." (Ex. 2, '450 patent, col. 38, ll. 65-67.)

74. The specification of the '450 and '110 patents describes DEET, which is the active compound in some insect repellants, as a "toxin." (Ex. 2, '450 patent, col. 35, ll. 48-55; Ex. 14, '110 patent, col. 39, ll. 49-56.) The '450 patent states in relevant part:

- "The environmental toxins selected for use in the study were . . . DEET, i.e. N,N-diethyl-m-toluamide (in the form of Deep woods OFF!® pump spray . . . ." (Ex. 2, '450 patent, col. 35, ll. 48-52.)
- "The Test Item and the controls were supplied ready-to-use. Toxin No. I (sunscreen) was applied undiluted. Toxins Nos. 2 (DEET) and 3 (2,4-D) were diluted in ethanol and water, respectively, ..." (Ex. 2, '450 patent, col. 36, ll. 13-16.)
- "Due to limitation in the sensitivity of the analytical methods employed in the study, no DEET (Toxin no. 2) or 2,4-D (Toxin no. 3) could be quantified in plasma for any of the animals . . . . A subsequent study (described in Example 3 below) using higher concentrations of DEET and 2,4-D was therefore conducted." (Ex. 2, '450 patent, col. 38, ll. 31-39.)
- "Results also showed that there was no quantifiable systemic absorption of DEET or 2,4-D at baseline . . . or following a 15-day pre-treatment . . . ." (Ex. 2, '450 patent, col. 39, ll. 6-10.)

VI. THE ACTAVIS ANDA PRODUCT

A. Overview

75. [redacted]

76. ANDA No. 207238 seeks the FDA's approval of diclofenac sodium topical solution, 2% w/w (hereinafter, "Actavis ANDA product"). [redacted]; No. 14-cv-7992, Dkt. 1, Compl. ¶ 46.)

77. Actavis is a pharmaceutical company that does not, and will not, engage in treating patients with topical products. (Ex. 18, Pappagallo Dep. Tr. 253:16-255:5.)

78. [redacted]

79. Diclofenac sodium is a type of non-steroidal anti-inflammatory drug ("NSAID"). (Ex. 16, Pappagallo Rep. ¶¶ 3, 20; Ex. 24, Pappagallo Resp. Rep. ¶ 150.)

80. Diclfoenac sodium was first synthesized in 1973 and is available in varying concentrations in several topical medications, including Voltaren® (1%), Flector® (1.3%), Pennsaid (1.5% and 2%), and Solaraze® (3%). (Ex. 24, Pappagallo Resp. Rep. ¶¶ 215-16, 226-28, 231-33, 242,

81. [redacted]

B. Labeling for Actavis's Proposed ANDA Product

82. [redacted]

83. [redacted]

84. [redacted]

85. [redacted]

86. [redacted]

87. [redacted]

88. [redacted]

89. [redacted]

90. [redacted]

91. [redacted]

92. [redacted]

93. Dr. Pappagallo admitted that Actavis's ANDA product is not indicated for use with a second drug or topical substance. (Ex. 18, Pappagallo Dep. Tr. 225:17-226:19.)

94. [redacted]

[redacted]

VII. HORIZON'S FAILURE TO IDENTIFY ANY INSTANCE OF DIRECT INFRINGEMENT

96. Horizon's infringement contentions do not identify any instance in which any person has used Pennsaid 2% in combination with any second topical substance. (Ex. 6, July 13, 2015 Horizon Infringement contentions, pp. 3 & Ex. A; Ex. 28, Oct. 15, 2015 Horizon Infringement Contentions, pp. 4 & Ex. A.)

97. The only allegation of direct infringement in Horizon's infringement contentions for the claims requiring application of more than one topical substance is that "[i]f Defendant's ANDA product is approved, [the asserted claims of the '078, '450, and '164 patents] . . . would be directly infringed at least by users of Defendant's ANDA Product who use same as directed by Defendant's proposed label." (Ex. 6, July 13, 2015 Horizon Infringement Contentions, p. 5; Ex. 28, Oct. 15, 2015 Horizon Infringement Contentions, pp. 4 & Ex. A.)

98. Horizon's infringement contentions do not allege that Actavis itself will treat a patient with both topical diclofenac and a second topical substance. (Ex. 6, July 13, 2015, Horizon Infringement Contentions, p. 5; Ex. 28, Oct. 15, 2015 Horizon Infringement Contentions, pp. 4 & Ex. A.)

99. Dr. Pappagallo testified that he does not contend that Actavis directly infringes the asserted method patents:

[redacted]

100. As stated in his June 30, 2016 report, the entirety of Dr. Pappagallo's infringement analysis for the limitations of the '078, '450, and '110 patents requiring the use of a second topical substance consists of some quotes from Actavis's labeling and the following statement, [redacted]

101. In Dr. Pappagallo's August 15, 2016 reply report, Dr. Pappagallo again makes no representation that any patient ever actually used both Pennsaid 2% and a second topical substance. [redacted]

102. Dr. Pappagallo never makes any assertion in his August 15, 2016 report that patients or doctors will likely use Actavis's ANDA product as well as a second topical substance once Actavis's ANDA is approved. (*See* Ex. 16, Pappagallo Rep. ¶ 46.)

103. In his reply report, Dr. Pappagallo suggests that he may have instructed patients about the labeling for either Pennsaid 1.5% or 2%, but does not state which product these instructions pertained to or whether any patient ever performed the claimed method in response to these purported instructions. [redacted]

[redacted]

104. [redacted]

[redacted]

105. [redacted]

[redacted]

- [redacted]
- [redacted]
- [redacted]

[redacted]

106. [redacted]

107. Neither Horizon's contentions nor Dr. Pappagallo's June 30, 2016 and August 15, 2016 reports make any allegation that a patient will necessarily use both Actavis's ANDA product and a second topical substance. (Ex. 6, July 13, 2015, Horizon Infringement Contentions, pp. 3, Ex. A at 43-51; Ex. 16, Pappagallo Rep. ¶¶ 47-48 & Ex. 16, pp. 1-14, 23-42; Ex. 20, Pappagallo Reply Rep. ¶¶ 48-51.)

1. [redacted]

108. Horizon designated its Chief Medical Officer, Dr. Jeffrey W. Sherman, to testify on the following topic related to the use of topical diclofenac products:

> 28. Horizon's awareness of any persons instructing others to use PENNSAID® 2%, or using PENNSAID® 2%, in combination with an oral NSAID or other topical products or medications, including but not limited to minoxidil, corticosteroid, sunscreen, insect repellent, herbicide, tretinoin, a topical NSAID, or a herbicide.

(Ex. 29, 30(b)(6) Topics, ¶¶ 26-28; Ex. 27, Sherman Dep. Tr. 133:6; Ex. 30, March 11, 2016, Email Witte to Lydigsen re: Sherman 30(b)(6) topics.)

109. [redacted]

110. [redacted]

[redacted]

112. Dr. Sherman's testimony concerning Horizon's lack of knowledge of persons instructing others to use Pennsaid 2% in combination with other substances was as follows:

[redacted]

[redacted]

113. [redacted]

[redacted]

2. Dr. Pappagallo's Lack of Knowledge of Any Combined Use of Topical Diclofenac Sodium with other Topical Substances

114. Dr. Pappagallo admitted that he had no knowledge of whether any person had ever applied both Pennsaid 1.5% or Pennsaid 2% and a second topical to their knee during the course of treatment. (Ex. 18, Pappagallo Dep. Tr. 218:22-219:2, 275:19-276:23.)

115. Dr. Pappagallo testified that he was unaware of whether any patient had ever applied Pennsaid 2% along with a second topical substance:

Q And for any of those patients that you've prescribed either Pennsaid 1.5 percent or 2 percent to, have you discussed with them applying a second topical?

A Again, as -- as need -- according to the needs. So I give the instruction. I'm not saying there is a need to another -- for another topical. I never, so . . .

Q Do you -- Do you remember whether you discussed applying a second topical with any of those patients?

A That I made a recommendation?

Q Do you remember whether you discussed applying a second topical with any of those patients?

A As I said, I gave the instruction. I don't -- I didn't recommend any other second. I didn't say you have to apply, let's say, steroids, because it doesn't make any sense. It's all according to the need.

Q Do you remember whether any of your patients indicated they had a need to apply a second topical?

A No.

Q And that includes sunscreens and insect repellents, right?

A I don't know. Yeah. I don't know. I don't have a follow-up on what they have done after my instructions.

(Ex. 18, Pappagallo Dep. Tr. 275:19-276:23.)

116. Dr. Pappagallo further testified:

Q You don't know whether any patient you've prescribed or recommended the use of Pennsaid for has actually put a second topical on their knee, do you?

A I don't -- I don't know that.

(Ex. 18, Pappagallo Dep. Tr. 218:22-219:2.)

VIII. HORIZON'S ALLEGATIONS OF INDUCED INFRINGEMENT

A. Dr. Pappagallo's Opinion Regarding Actavis's Labeling

117. On June 30, 2016 and October 6, 2016, Dr. Marco Pappagallo, M.D., submitted expert reports in which he opines, *inter alia*, "that the use of Actavis' ANDA product in accordance with Actavis' proposed labeling would infringe the asserted claims of the patents-in-suit literally or under the doctrine of equivalents." (Ex. 16, Pappagallo Rep. ¶ 16.)

118. In addition to the copy of Actavis's labeling at ACT-PENN0045016-42 (Ex. 26, 2016 Actavis Label), Dr. Pappagallo also cites the side-by-side comparison between Actavis's labeling for ANDA No. 207238 and the labeling for Pennsaid 2% at ACT-PENN0045044-83.

[redacted]

121. [redacted]

122. Dr. Pappagallo testified:

[redacted]

(Ex. 18, Pappagallo Dep. Tr. 209:13-210:17.)

123. [redacted]

124. [redacted]

125. [redacted]

126. [redacted]

127. [redacted]

128. [redacted]

129. [redacted]

132. [redacted]

133. In his reply report, Dr. Pappagallo identified [redacted] as being relevant to his views of induced infringement. (Ex. 26, 2016 Actavis Label, ACT-PENN0045024; Ex. 20, Pappagallo Reply Rep. ¶ 49.)

134. Dr. Pappagallo did not cite to [redacted] in his opening report, dated June 30, 2016. (Ex. 16, Pappagallo Rep.)

135. [redacted]

138. During his deposition, Dr. Pappagallo identified [redacted] as relevant to his view that Actavis's proposed labeling will induce patients to use Actavis's ANDA product with a topical corticosteroid. (Ex. 18, Pappagallo Dep. Tr. 340:3-16.)

139. Dr. Pappagallo never identified [redacted] as relevant to his opinion of induced infringement in his expert reports. (Ex. 16, Pappagallo Rep.; Ex. 20, Pappagallo Reply Rep.)

140. [redacted]

141. [redacted]

142. [redacted]

143. [redacted]

144. [redacted]

145. [redacted]

146. [redacted]

147. Moisturizers are a common way to treat dry skin. (Ex. 18, Pappagallo Dep. Tr. 340:7-8.)

148. [redacted]

B. [redacted]

149. [redacted]

150. [redacted]

[redacted]

151. Horizon designated Dr. Sherman to testify on the following topic related to the labeling for PENNSAID 2%:

> 27. The labeling and package insert for PENNSAID® 2%, including, but not limited to, statements in the labeling and/or package insert relating to: (i) the method, location, and instructions for application of PENNSAID® 2%; (ii) the use of PENNSAID® 2% with other substances and medications, including sunscreen, insect repellent, cosmetics, lotions, moisturizer, topical medications, corticosteroids, or oral NSAIDs; (iii) the reasons for including any of the foregoing statements in the labeling and/or package insert; and (iv) communications with the FDA regarding the use of PENNSAID® 1.5% or PENNSAID® 2% with other substances and medications, including sunscreen, insect repellent, cosmetics, lotions, moisturizer, topical medications, corticosteroids, or oral NSAIDs.

(Ex. 29, 30(b)(6) Topics, ¶¶ 26-28; Ex. 27, Sherman Dep. Tr. 133:6; Ex. 30, March 11, 2016, Email Witte to Lydigsen re: Sherman 30(b)(6) topics.)

152. [redacted]

153. [redacted]

- [redacted]
- [redacted]
- [redacted]

[redacted]

154. [redacted]

[redacted]

[redacted]

C. Dr. Pappagallo's Admissions That Any Use Of A Second Topical Would Be Based On Patient Needs Rather Than Actavis's Labeling

156. Dr. Pappagallo testified that his opinion of infringement is based on patients applying a second topical substance due to a "medical need" rather than an instruction in Actavis's labeling. (Ex. 18, Pappagallo Dep. Tr. 215:3-5, 216:7-23, 217:10-220:2, 238:8-12, 243:11-244:12, 280:14-281:4, 283:3-11.)

157. [redacted]

158. [redacted]

D. Dr. Pappagallo Failed To Consider Specific Intent When Forming His Opinion Of Induced Infringement

159. Dr. Pappagallo testified that he did not consider specific intent in forming his opinion that Actavis's labeling will induce infringement. (Ex. 18, Pappagallo Dep. Tr. 241:15-244:12.)

160. Dr. Pappagallo testified:

Q Did you consider Actavis' specific intent when you did your analysis here?

A No, I didn't.

(Ex. 18, Pappagallo Dep. Tr. 244:10-12.)

E. Dr. Pappagallo's Agreement That Conditional Precautions Do Not Induce The Activity Subject To The Cautionary Statement

161. [redacted]

162. [redacted]

163. [redacted]

164. [redacted]

165. [redacted]

166. [redacted]

F. [redacted]

167. [redacted]

168. [redacted]

169. [redacted]

170. [redacted]

171. [redacted]

172. [redacted]

173. [redacted]

IX. ACTAVIS'S ANDA PRODUCT HAS SUBSTANTIAL NON-INFRINGING USES

174. Horizon's 30(b)(6) witness did not provide any testimony one way or the other as to whether it is possible that at least some patients use Pennsaid 2% without applying a second topical product such as minoxidil, corticosteroid, sunscreen, insect repellent, herbicide, tretinoin, a topical NSAID, or a herbicide. (Ex. 27, Sherman Dep. Tr. 170:5-171:1.)

175. Dr. Thomas Zizic is a rheumatologist who practices at The Johns Hopkins Hospital and Good Samaritan Hospital in Baltimore, Maryland. (Ex. 33, Zizic Opening Rep. at Ex. 1 Curriculum Vitae.) Dr. Zizic has over 45 years of experience in treating patients with osteoarthritis and has submitted an expert report on behalf of Actavis in which he opines that Actavis's ANDA has substantial uses that do not infringe any of the methods set forth in the asserted claims of the '450, '078, '164, and '110 patents. (Ex. 34, Zizic Reb. Rep. ¶¶ 45-50, 73.)

176. Dr. Zizic submitted an expert report on behalf of Actavis in which he opines:

> I have also been asked to consider whether the Actavis ANDA Product has substantial uses [redacted] It is my opinion that the Actavis ANDA Product, when used in accordance with the Actavis Labeling, will have substantial uses that will not infringe the Asserted Method Claims that require the foregoing steps. For example, as described in Paragraphs 46-49, physicians will understand that the Actavis ANDA Product can be applied as a monotherapy or in combination with non-topical modalities, without the subsequent application of any additional topical agents. Indeed, I frequently

> prescribe Pennsaid 2% in my practice, and I have *never* instructed a patient to apply a second topical agent of any kind during a course of treatment with Pennsaid 2%.

(Ex. 34, Zizic Reb. Rep. ¶ 73.)

177. Dr. Zizic submitted an expert report on behalf of Actavis in which he opines that Actavis's ANDA Product can be used as a monotherapy:

> [redacted]
>
> . . . .
>
> In addition, numerous published studies involving Pennsaid 1.5% demonstrate that Pennsaid 1.5% was also effective as monotherapy and therefore provide further support for the effectiveness of Pennsaid 2% as a monotherapy.[14]

(Ex. 34, Zizic Reb. Rep. ¶¶ 46, 47.) Dr. Zizic identified a number of published studies in which Pennsaid 1.5% or 2% were used as monotherapies in footnote 14 of his report:

> *See e.g.* P.A. Baer, et al., *Treatment of Osteoarthritis of the Knee with a Topical Diclofenac Solution: A Randomized Controlled, 6-week Trial*, 6 BMC Musculoskeletal Disorders 44 (2005) (ACT-PENN0010945 – ACT-PENN0010953); Sanford H. Roth, et al., *Efficacy and Safety of a Topical Diclofenac Solution (Pennsaid) in the Treatment of Primary Osteoarthritis of the Knee*, 164 ARCHIVES OF INTERNAL MED. 2017 (2004) (ACT-PENN0011766 – ACTPENN0011773); Peter S. Tugwell, et al., *Equivalence Study of a Topical Diclofenac Solution (Pennsaid®) Compared with Oral Diclofenac in Symptomatic Treatment of Osteoarthritis of the Knee: A Randomized Controlled Trial*, 31 J. RHEUMATOLOGY 2002 (2004) (ACTPENN0011900- ACT-PENN0011910); J. Zacher, et al., *Topical Diclofenac and Its Role in Pain and Inflammation: An Evidence-Based Review*, 24 CURRENT MEDICAL RESEARCH & OPINION 24 (2008) 925 (ACT-PENN0045622 – ACT-PENN0045648); Lee S. Simon, et. al., *Efficacy and safety of topical diclofenac containing dimethyl sulfoxide (DMSO) compared with those of topical placebo, DMSO vehicle and oral diclofenac for knee osteoarthritis,* 143 PAIN 238 (2009) (HNZPENN_00030759 - HZNPENN_00030766); Moen, *Topical Diclofenac Solution*, 69 Drugs 2621

> (2009) (HZNPENN_00144724 - HZNPENN_00144735); T.E. Towheed, *Pennsaid® Therapy for Osteoarthritis of the Knee: A Systematic Review and Metaanalysis of Randomized Controlled Trials*, 33 J. RHEUMATOLOGY 567 (2006) (ACTPENN0011892 – ACT-PENN0011899); Arther A.M. Bookman, et al., *Effect of a topical diclofenac solution for relieving symptoms of primary osteoarthritis of the knee: a randomized controlled trial*, 171 CMAJ 333 (2004) (ACT-PENN0013547 - ACT-PENN0013552).

(Ex. 34, Zizic Reb. Rep. ¶ 47 n.14.)

178. Dr. Zizic submitted an expert report on behalf of Actavis in which he opines that Actavis's ANDA Product can be used in combination with non-pharmacological remedies:

> For example, the Actavis ANDA Product may also be administered in combination with non-pharmacological remedies such as physical therapy, walking aids, correction of mal-alignment through the use of a supportive brace, specialized footwear, and thermal modalities. (*See* Zizic Invalidity Rpt. at ¶24; *see also* Bruyere at 256 tble.2.)

(Ex. 34, Zizic Reb. Rep. ¶ 48.)

179. Dr. Zizic submitted an expert report on behalf of Actavis in which he opines that Actavis's ANDA Product can be used in combination with pharmacological treatments:

> As discussed in Bruyere, topical NSAIDs, such as the Actavis ANDA product, can also be used in combination with pharmacological treatments other than oral NSAIDs, such as acetaminophen (paracetamol) or nutraceuticals, e.g., glucosamine, chondroitin sulfate, avocado soybean unsaponifiables, etc. (*see, e.g.*, Bruyere at Abstract, 256 fig., 258, 260), or intra-articular corticosteroid or hyaluronic acid injections (*see, e.g.*, Bruyere at 259). Topical NSAIDs, such as the Actavis ANDA Product, also can be administered in combination with narcotic analgesics, such as tramadol and opioids.

(Ex. 34, Zizic Reb. Rep. ¶ 49.)

180. Dr. Zizic submitted an expert report on behalf of Actavis in which he opines:

> In my own clinical experience, and based on my expert understanding of the standard of care for treating osteoarthritis of the knee, the majority of patients treated with a topical diclofenac sodium product (such as the Actavis ANDA Product) for osteoarthritis of the knee, localized or generalized, are treated with one or more of the above treatments – monotherapy, combination therapy with a non-pharmacological therapy, and/or combination therapy with a pharmacological

> therapy other than an oral NSAID – not with a combination of topical diclofenac sodium and an oral NSAID.

(Ex. 34, Zizic Reb. Rep. ¶ 50.)

181. Dr. Pappagallo's expert reports in this case do not address contributory infringement. (Ex. 16 Pappagallo Rep.; Ex. 20, Pappagallo Reply Rep.)

182. Dr. Pappagallo's expert reports in this case contain no mention of the terms "substantial noninfringing use" or "staple article." (Ex. 16, Pappagallo Rep.; Ex. 20, Pappagallo Reply Rep.)

183. At deposition, Dr. Pappagallo testified that he had no knowledge of whether a substantial number of persons would use Pennsaid without a second topical product on their knee:

> Q Would you agree that a substantial number of the people that are applying Pennsaid are not going to put a second topical product on their knee?
>
> MR. GRIFFITH: Objection, foundation, form, incomplete hypothetical.
>
> A I'm unaware. I don't know.

(Ex. 18, Pappagallo Dep. Tr. 218:2-8.)

184. Dr. Pappagallo acknowledged that many patients will have no need to use Actavis's ANDA product with sunscreen, insect repellent, or a second topical medication. (Ex. 18, Pappagallo Dep. Tr. 215:12-218:1.)

185. There is no dispute that at least persons living in the Northern half of the United States would have no reason to apply sunscreen or insect repellent to their knee for a good portion of the year. (Ex. 18, Pappagallo Dep. Tr. 220:3-8, 221:2-10.)

186. Dr. Pappagallo testified:

> Q Would you agree that for a good portion of the year the people in the northern half of our country, the United States, would not have any reason to apply sunscreen or insect repellent to their knee?

A Yes, I agree.

Q Would you agree that a substantial number of users of topical diclofenac sodium 2 percent are not going to have any reason to apply sunscreen or insect repellent for a good chunk of the year?

MR. GRIFFITH: Objection, form.

A Yeah. That I can--I don't know about that. But frankly, as a physician, I said anyhow.

BY MS. LYDIGSEN

Q You said what?

A I give instruction anyhow. I'm not basing my instruction based on the fact, oh, this patient will never put shorts. I mean that's not good medicine.

Q You work in New York, right?

A Yes.

Q So do you recommend a lot of sunscreen, insect repellent in mid-January?

A In the summertime, yes.

Q But not in January, right?

A Not in January.

Q And your patients aren't asking you about sunscreen, insect repellent in January, I would think either?

A. In January, probably not.

(Ex. 18, Pappagallo Dep. Tr. 220:3-221:10.)

187. Dr. Pappagallo further testified:

Q Is it an instruction -- Is this an instruction that a patient should apply sunscreen?

MR. GRIFFITH: Asked and answered.

BY MS. LYDIGSEN:

Q You can answer it again.

A The sunscreen is, in my opinion, medically necessary for that particular patient, for the patient who expose the skin after treatment.

Q But what about a patient who is wearing pants, is the sunscreen necessary for them?

A No.

Q So it's not really medically necessary unless there are other conditions present, right?

A Yes. I mean unless you are in a situation where you don't wear clothing.

[redacted]

X. PENNSAID 2% LABELING LANGUAGE

188. Actavis's ANDA No. 207238 seeks approval for diclofenac sodium topical solution 2% w/w [redacted] (No. 14-7992, Dkt. 1, Compl., ¶ 47; 21 C.F.R. § 314.3(b).)

189. FDA regulations require that the drug product labeling "must contain the specific information required under [21 C.F.R. §] 201.57(a), (b), and (c) under [particular] headings and subheadings and in [particular] order." 21 C.F.R. § 201.56(d)(1).

190. An ANDA must contain proposed labeling that is the "same as the labeling approved for the [reference] listed drug" subject to a few exceptions, such as revisions to reflect that the "new drug and the listed drug are produced or distributed by different manufacturers." (*See* 21 U.S.C. § 355(j)(2)(A)(v); 21 C.F.R. § 314.127(a)(7), 314.94(a)(8)(iii)-(iv).)

191. [redacted]

192. [redacted]

193. [redacted]

194. [redacted]

195. [redacted]

196. [redacted]

197. [redacted]

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